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Effect of magnesium on arrhythmia incidence in patients undergoing coronary artery bypass grafting

Alireza Mohammadzadeh, Farshad Towfighi and Naser Jafari
Department of Cardiothoracic, Imam Khomeini Hospital, Ardabil University of Medical Sciences, Ardabil, Iran

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arrhythmia, coronary artery bypass grafting, hypomagnesaemia, magnesium sulphate.

Correspondence
Dr Alireza Mohammadzadeh, Department of Cardiothoracic, Imam Khomeini Hospital, Atayi Street, Ardabil University of Medical Sciences, Ardabil 56197, Iran. Email: a.mohammadzadeh@arums.ac.ir

A. Mohammadzadeh MD; **F. Towfighi** MD; **N. Jafari** PhD.

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Abstract

Background: Cardiac arrhythmia after coronary artery bypass grafting (CABG) surgery is a common complication of cardiac surgery. The effect of serum magnesium, hypomagnesaemia treatment and prophylactic administration of magnesium in the development and prevention of arrhythmias is controversial and there are many different ideas. This study evaluates the therapeutic effects of magnesium in cardiac arrhythmia after CABG surgery.
Methods: The clinical trial enrolled 250 patients who underwent CABG. Based on the initial serum levels of magnesium, patients were divided into two groups: hypomagnesium and normomagnesium. Based on bioethics committee requirements, patients in the hypomagnesium group received magnesium treatments until they attained normal magnesium blood levels. Both groups underwent CABG with normal blood levels of magnesium. After surgery, each group was randomly divided into two subgroups: one subgroup received a bolus dose of magnesium sulphate (30 mg/kg in 5 min) and the other subgroup received a placebo. Subgroups were under observation in the intensive care unit for 3 days and arrhythmias were recorded. Data from all four subgroups were analysed statistically and interpreted.
Results: The results of this study showed that the occurrence of arrhythmia was not significantly different among subgroups ($P > 0.05$). There was no significant relationship between blood levels of magnesium and arrhythmia during the 3 days post-surgery ($P > 0.05$).
Conclusion: The results of this study showed that magnesium sulphate administration did not significantly improve the incidence of arrhythmias in hypo- and normo-magnesium patients after CABG. There was no significant correlation between post-operative serum levels of magnesium and arrhythmia during 3 days.

Introduction

Cardiovascular system disorders are some of the most important health problems. A large number of cardiac patients undergo cardiac surgery, and coronary artery bypass grafting (CABG) is especially common. CABG is an 'open heart surgery in which a section of a blood vessel is grafted from the aorta to the coronary artery to bypass the blocked section of the coronary artery and improve the blood supply to the heart'. Nowadays, myocardial revascularization is the most accepted operation performed by cardiac surgeons.[1,2] Because CABG is implemented widely by surgeons, expanding the current knowledge of this operation could enrich efficacy and life expectancy in patients.

CABG is associated with many perioperative complications, including supraventricular and ventricular arrhythmias and conduction disturbances.[3,4] Arrhythmias are major complications after cardiac surgery, and can lead to morbidity and mortality, increased length of hospital stay and economic expenses.[3,5]

Various medications have been suggested to control arrhythmias. In some cases, antiarrhythmic drugs or electrical cardioversion could be administered. Magnesium sulphate (MGS) solution has been used as an adjuvant medication in anaesthesia for numerous different purposes. It has been administered in surgical patients as an analgesic and in cardiac operation patients as an anti-inflammatory agent.[6–9] It has been demonstrated that the administration of MGS could decrease the incidence of post-operative atrial fibrillation (AF) in cardiac surgery patients.[10–12]

To date, there is no conclusive evidence about the effectiveness of MGS on alleviating arrhythmias in patients who underwent CABG surgery. Therefore, this study explores the possible effects of MGS on reducing arrhythmias in patients after CABG.

Patients and methods

The controlled clinical trial enrolled 250 patients who underwent CABG. The ethics committee of Human Research at Ardabil University of Medical Sciences (Human Bioethics Committee) approved the study. Iranian Registry of Clinical Trials (IRCT), which is one of the certified Primary Registries in the WHO Registry Network, registered this clinical trial with the number of 'IRCT2015092224133N1'. Moreover, all patients gave an informed written consent before enrolment.

Based on the initial blood level of magnesium, patients were allocated into one of the two groups of hypomagnesium and normomagnesium. According to recommendations of IRCT and also requirements from Human Bioethics Committee, hypomagnesium patients should have normal blood level of magnesium before undergoing cardiac operation. Therefore, in order to fulfil the requirements and comply with human bioethics criteria, patients in the hypomagnesium group received MGS to attain normal blood level of magnesium (1.7–2.2 mg/dL).

Both groups underwent surgery with normal blood levels of magnesium. In order to elucidate the efficacy of post-operative magnesium therapy on the incidence of cardiac arrhythmias after CABG, both groups should be divided into two: placebo and MGS-administered subgroups.

Therefore, after surgery, both groups were randomly divided into two subgroups: subgroup #1 (placebo subgroup) received a normal saline with the same volume and the same infusion model as treatment, and subgroup #2 (MGS subgroup) received a bolus dose of MGS (30 mg/kg in 5 min).

The blood samples of patients were collected and each patient was given a specific code.

One of the project team members gathered the data from patients in the intensive care unit; she was blinded regarding the categorization of groups and subgroups. Subgroups were under observation for 3 days in the intensive care unit and arrhythmias were recorded.

Statistical analysis

Statistical analysis was performed using a graph and data analysis software package (SigmaPlot 12.0, Systat Software, Inc., San Jose, CA, USA). Data are presented as mean ± SD, except in figures where error bars represent SEM. Analysis of variance tests followed by chi-square test for multiple comparisons were performed to check the differences. P-value <0.05 was considered significant.

A power calculation was done to ascertain whether sufficient numbers of patients would make significant difference between the groups. The calculation estimated that a sample size of 55 patients in each group completing the study would allow us to detect a significant difference with 95% power with an alpha value of 0.05 (a 5% chance of incorrectly accepting the hypothesis).

Results

Demographic variables (including gender, age, body mass, serum creatinine, history of previous diabetes, β-blockers therapy, diuretic therapy and antiarrhythmia therapy) were measured and analysed in hypo- and normo-magnesium groups. There was no recorded case of mortality or morbidity in the two groups of patients in this study. There were no significant differences between the two groups with regard to preoperative parameters (Table 1). Serum levels of electrolytes were between the normal ranges during the study.

Serum magnesium levels of the patients in the four subgroups were analysed and compared with each other (Table 2). There was no significant difference between subgroups in 24, 48 and 72 h time points after operation.

Patients were monitored and prevalence of arrhythmias was recorded for 3 days after CABG. Because of high incidence of AF and premature ventricular contractions, these were reported separately. However, other types of arrhythmia were documented as one category (Table 3).

The incidence of arrhythmias was measured for the period of 3 days after surgery. Based on chi-square test, there was no significant difference between subgroups in three time points ($P > 0.05$, Table 4).

In order to elucidate the relevance of blood magnesium with the incidence of arrhythmias, serum levels of magnesium were measured at three time points after surgery (Table 5).

Discussion

MGS inhibits the release of catecholamines from adrenal medulla and peripheral nerve endings and directly blocks receptors of catecholamines.[13] Therefore, MGS causes sympathetic block which causes dilated blood vessels and, consequently, reduces blood pressure.[14–17] It has been reported that administration of MGS solution could suppress part of the inflammatory response after CABG.[18,19] Another study has demonstrated that intravenous MGS could decrease the serum levels of post-operative N-terminal pro-brain natriuretic peptide in elective CABG.[20] MGS might be

Table 1 Demographics and characteristics

Variable	Hypomagnesium	Normomagnesium	*P*-value
Age (years old)	60.8 ± 7.6	61.3 ± 6.6	0.41
Male	64.5	58.6	0.72
Female	35.5	41.4	0.65
Cardiac cachexia	16.5	17.8	0.86
History of previous diabetes	35.3	10.6	0.56
Serum creatinine	1.2 ± 0.5	1.2 ± 0.3	0.47
β-Blockers therapy	71.6	69.4	0.51
Diuretic therapy	62.8	60.4	0.84
Antiarrhythmia therapy	25.5	25.5	0.5

Table 2 Serum magnesium levels in hypo- and normo-magnesium groups and relevant subgroups (mean ± SD)

	Hypomagnesium		*P*-value	Normomagnesium		*P*-value
	Placebo	Prophylaxis		Placebo	Prophylaxis	
First day	1.82 ± 0.14	2.36 ± 0.12	0.001	1.75 ± 0.18	2.15 ± 0.21	0.001
Second day	1.67 ± 0.14	2.24 ± 0.13	0.001	1.62 ± 0.19	2.92 ± 0.25	0.001
Third day	1.45 ± 0.15	2.08 ± 0.14	0.001	1.45 ± 0.17	2.76 ± 0.22	0.001

Table 3 Incidence of arrhythmias at three time points after CABG. Because of high incidence of AF and PVCs, these are reported separately

	Day 1	Day 2	Day 3
Without arrhythmia	178 (71.2%)	184 (73.6%)	167 (66.8%)
AF	40 (16%)	41 (16.4%)	48 (19.2%)
PVCs	28 (11.2%)	23 (9.2%)	30 (12%)
Other arrhythmias	4 (1.6%)	2 (0.8%)	5 (2%)

AF, atrial fibrillation; CABG, coronary artery bypass grafting; PVC, premature ventricular contraction.

Table 4 Comparison of arrhythmia incidence in different subgroups at three time points after CABG. Data are presented as percentile of the patients in each subgroup at specific time point

	Arrhythmia incidence	Hypomagnesium		Normomagnesium		*P*-value
		Placebo	Prophylaxis	Placebo	Prophylaxis	
Day 1	+	37.4	21	32.5	16.9	0.38
	−	62.6	79	67.5	83.1	0.45
Day 2	+	29.2	27.8	22.9	20	0.72
	−	70.8	72.2	77.1	80	0.23
Day 3	+	40.8	31.3	33.6	24.4	0.69
	−	59.2	68.7	66.4	75.6	0.45

CABG, coronary artery bypass grafting.

effective in regulating haemodynamics, while it may increase the heart rate.[21] It is considered as a medication for the treatment of pre-eclampsia and blood pressure management.[22–24]

To date, there is no consensus protocol in administration of MGS to prevent the incidence of cardiac arrhythmias after CABG. The discrepancy between surgeons may in part be due to implication of different methods of MGS administration.

Even though it has been suggested that N-acetylcysteine and magnesium decreased pump-induced oxidative stress during cardiopulmonary bypass,[10,25] our data suggest that MGS might not have any effect in reducing post-operative arrhythmias.

Our results demonstrated that there were no differences in the incidence of arrhythmias at three time points after CABG. Administration of MGS did not improve the occurrence of arrhythmias in hypomagnesium patients for whom serum magnesium levels were adjusted before operation, or in normomagnesium patients who needed no serum magnesium adjustment before surgery. Moreover, there was no significant correlation between post-operative serum levels of magnesium and arrhythmia during 3 days ($P > 0.05$).

Table 5 Serum magnesium (mg/dL) levels after CABG (mean ± SD)

Serum magnesium	Without arrhythmia	Arrhythmias	*P*-value
Day 1	2.35 ± 0.7	2.15 ± 0.8	0.22
Day 2	2.19 ± 0.8	2.07 ± 0.7	0.92
Day 3	1.96 ± 0.6	1.8 ± 0.5	0.78

CABG, coronary artery bypass grafting.

Results of several studies are in agreement with our findings. Outcomes of a randomized clinical trial revealed that prophylactic intravenous MGS in addition to oral β-blockade did not prevent atrial arrhythmias after coronary artery or valvular heart surgery.[26]

A report that is published in the Cochrane Database Systematic Reviews analysed the data from 118 randomized controlled trials. Analysed interventions included amiodarone, beta-blockers, sotalol, magnesium, atrial pacing and posterior pericardiotomy. These interventions were effective in reducing the rate of post-operative AF after cardiac surgery compared with a control. However, magnesium's efficacy reported to be slightly less.[27] Another meta-analysis that focused on well-conducted, five double-blind, intention-to-treat studies showed that the prophylactic use of magnesium did not prevent post-operative AF.[28]

Interestingly, another meta-analysis suggested that magnesium had no effect on the incidence of post-operative stroke, myocardial infarction and death. Moreover, it mentions that magnesium did not decrease the hospital or intensive care unit lengths of stay. This study suggested that in higher quality studies MGS did not reduce post-operative supraventricular arrhythmias significantly.[29]

In contrast, a meta-analysis study of 2490 patients reported that magnesium administration reduced the incidence of developing post-operative AF from 28% in the control group to 18% in the treatment group; however, it did not significantly decrease hospital length of stay or mortality.[30] However, another meta-analysis revealed that magnesium administration is not effective for reducing post-operative atrial arrhythmias, hospital length of stay and mortality after CABG.[31] These reports support our findings and add evidence against the prophylactic administration of magnesium for prevention of arrhythmias after CABG.

Conclusion

The results of this clinical trial add evidence against the effectiveness of MGS for prevention of arrhythmias after CABG. The incidence of arrhythmias in MGS-administered subgroups was not significantly different from placebo-administered subgroups. There was no significant correlation between serum levels of magnesium and arrhythmia during 3 days post-operation.

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